

SEQUENCE LISTING

<110> RATAIN, MARK J.
INNOCENTI, FEDERICO
DAS, SOMA
IYER, LALITHA
SAWYER, MICHAEL

<120> COMPOSITIONS AND METHODS FOR OPTIMIZING UGT2B7 SUBSTRATE DOSINGS
AND FOR
PREDICTING UGT2B7 SUBSTRATE TOXICITY

<130> ARCD:358US

<150> UNKNOWN

<151> 2002-01-25

<140> 60/264,534

<141> 2001-01-26

<160> 78

<170> PatentIn Ver. 2.1

<210> 1

<211> 1991

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (151)..(1740)

<400> 1

catgctcaga ctgttgattt aatgatattg tatgtacttt gacttataag ggttacattt 60

taactttcttg gctaatttat ctttggacat aaccatgaga aatgacagaa aggaacagca 120

actggaaaac aagcattgca ttgcaccagg atg tct gtg aaa tgg act tca gta 174
Met Ser Val Lys Trp Thr Ser Val

1

5

att ttg cta ata caa ctg agc ttt tgc ttt agc tct ggg aat tgt gga 222
Ile Leu Leu Ile Gln Leu Ser Phe Cys Phe Ser Ser Gly Asn Cys Gly

10

15

20

aag gtg ctg gtg tgg gca gca gaa tac agc cat tgg atg aat ata aag 270
Lys Val Leu Val Trp Ala Ala Glu Tyr Ser His Trp Met Asn Ile Lys

25

30

35

40

aca atc ctg gat gag ctt att cag aga ggt cat gag gtg act gta ctg 318
Thr Ile Leu Asp Glu Leu Ile Gln Arg Gly His Glu Val Thr Val Leu

45

50

55

3057341425004

gca tct tca gct tcc att ctt ttt gat ccc aac aac tca tcc gct ctt	366
Ala Ser Ser Ala Ser Ile Leu Phe Asp Pro Asn Asn Ser Ser Ala Leu	
60 65 70	
aaa att gaa att tat ccc aca tct tta act aaa act gag ttg gag aat	414
Lys Ile Glu Ile Tyr Pro Thr Ser Leu Thr Lys Thr Glu Leu Glu Asn	
75 80 85	
ttc atc atg caa cag att aag aga tgg tca gac ctt cca aaa gat aca	462
Phe Ile Met Gln Gln Ile Lys Arg Trp Ser Asp Leu Pro Lys Asp Thr	
90 95 100	
ttt tgg tta tat ttt tca caa gta cag gaa atc atg tca ata ttt ggt	510
Phe Trp Leu Tyr Phe Ser Gln Val Gln Glu Ile Met Ser Ile Phe Gly	
105 110 115 120	
gac ata act aga aag ttc tgt aaa gat gta gtt tca aat aag aaa ttt	558
Asp Ile Thr Arg Lys Phe Cys Lys Asp Val Val Ser Asn Lys Lys Phe	
125 130 135	
atg aaa aaa gta caa gag tca aga ttt gac gtc att ttt gca gat gct	606
Met Lys Lys Val Gln Glu Ser Arg Phe Asp Val Ile Phe Ala Asp Ala	
140 145 150	
att ttt ccc tgt agt gag ctg ctg gct gag cta ttt aac ata ccc ttt	654
Ile Phe Pro Cys Ser Glu Leu Leu Ala Glu Leu Phe Asn Ile Pro Phe	
155 160 165	
gtg tac agt ctc agc ttc tct cct ggc tac act ttt gaa aag cat agt	702
Val Tyr Ser Leu Ser Phe Ser Pro Gly Tyr Thr Phe Glu Lys His Ser	
170 175 180	
gga gga ttt att ttc cct cct tcc tac gta cct gtt gtt atg tca gaa	750
Gly Gly Phe Ile Phe Pro Pro Ser Tyr Val Pro Val Val Met Ser Glu	
185 190 195 200	
tta act gat caa atg act ttc atg gag agg gta aaa aat atg atc tat	798
Leu Thr Asp Gln Met Thr Phe Met Glu Arg Val Lys Asn Met Ile Tyr	
205 210 215	
gtg ctt tac ttt gac ttt tgg ttc gaa ata ttt gac atg aag aag tgg	846
Val Leu Tyr Phe Asp Phe Trp Phe Glu Ile Phe Asp Met Lys Lys Trp	
220 225 230	
gat cag ttt tat agt gaa gtt cta gga aga ccc act acg tta tct gag	894
Asp Gln Phe Tyr Ser Glu Val Leu Gly Arg Pro Thr Thr Leu Ser Glu	
235 240 245	
aca atg ggg aaa gct gac gta tgg ctt att cga aac tcc tgg aat ttt	942
Thr Met Gly Lys Ala Asp Val Trp Leu Ile Arg Asn Ser Trp Asn Phe	
250 255 260	
cag ttt cct cat cca ctc tta cca aat gtt gat ttt gtt gga gga ctc	990
Gln Phe Pro His Pro Leu Leu Pro Asn Val Asp Phe Val Gly Gly Leu	
265 270 275 280	

cac His	tgc Cys	aaa Lys	cct Pro	gcc Ala 285	aaa Lys	ccc Pro	ctg Leu	cct Pro	aag Lys 290	gaa Glu	atg Met	gaa Glu	gac Asp	ttt Phe 295	gta Val	1038
cag Gln	agc Ser	tct Ser 300	gga Gly	gaa Glu	aat Asn	ggg Gly	gtt Val	gtg Val 305	gtg Val	ttt Phe	tct Ser	ctg Leu	ggg Gly 310	tca Ser	atg Met	1086
gtc Val	agt Ser	aac Asn 315	atg Met	aca Thr	gaa Glu	gaa Glu	agg Arg 320	gcc Ala	aac Asn	gta Val	att Ile	gca Ala 325	tca Ser	gcc Ala	ctg Leu	1134
gcc Ala 330	cag Gln	atc Ile	cca Pro	caa Gln	aag Lys	gtt Val 335	ctg Leu	tgg Trp	aga Arg	ttt Phe	gat Asp 340	ggg Gly	aat Asn	aaa Lys	cca Pro	1182
gat Asp 345	acc Thr	tta Leu	ggg Gly	ctc Leu	aat Asn 350	act Thr	cgg Arg	ctg Leu	tat Tyr	aag Lys 355	tgg Trp	ata Ile	ccc Pro	cag Gln	aat Asn 360	1230
gac Asp	ctt Leu	cta Leu	ggg Gly	cat His 365	cca Pro	aag Lys	acc Thr	aga Arg	gct Ala 370	ttt Phe	ata Ile	act Thr	cat His	ggg Gly 375	gga Gly	1278
gcc Ala 380	aat Asn	ggc Gly	atc Ile	tac Tyr	gag Glu	gca Ala	atc Ile	tac Tyr 385	cat His	ggg Gly	atc Ile	cct Pro	atg Met 390	gtg Val	ggg Gly	1326
att Ile	cca Pro	ttg Leu 395	ttt Phe	gcc Ala	gat Asp	caa Gln	cct Pro 400	gat Asp	aac Asn	att Ile	gct Ala	cac His 405	atg Met	aag Lys	gcc Ala	1374
agg Arg 410	gga Gly	gca Ala	gct Ala	gtt Val	aga Arg	gtg Val 415	gac Asp	ttc Phe	aac Asn	aca Thr	atg Met 420	tcg Ser	agt Ser	aca Thr	gac Asp	1422
ttg Leu 425	ctg Leu	aat Asn	gca Ala	ttg Leu	aag Lys 430	aga Arg	gta Val	att Ile	aat Asn	gat Asp 435	cct Pro	tca Ser	tat Tyr	aaa Lys	gag Glu 440	1470
aat Asn	gtt Val	atg Met	aaa Lys	tta Leu 445	tca Ser	aga Arg	att Ile	caa Gln	cat His 450	gat Asp	caa Gln	cca Pro	gtg Val	aag Lys 455	ccc Pro	1518
ctg Leu	gat Asp	cga Arg	gca Ala 460	gtc Val	ttc Phe	tgg Trp	att Ile	gaa Glu 465	ttt Phe	gtc Val	atg Met	cgc Arg	cac His 470	aaa Lys	gga Gly	1566
gct Ala	aaa Lys	cac His 475	ctt Leu	cgg Arg	gtt Val	gca Ala	gcc Ala 480	cac His	gac Asp	ctc Leu	acc Thr	tgg Trp 485	ttc Phe	cag Gln	tac Tyr	1614
cac His	tct Ser	ttg Leu	gat Asp	gtg Val	att Ile	ggg Gly	ttc Phe	ctg Leu	ctg Leu	gtc Val	tgt Cys	gtg Val	gca Ala	act Thr	gtg Val	1662

490

495

500

ata ttt atc gtc aca aaa tgt tgt ctg ttt tgt ttc tgg aag ttt gct 1710
 Ile Phe Ile Val Thr Lys Cys Cys Leu Phe Cys Phe Trp Lys Phe Ala
 505 510 515 520

aga aaa gca aag aag gga aaa aat gat tag ttatatctga gatttgaagc 1760
 Arg Lys Ala Lys Lys Gly Lys Asn Asp
 525 530

tggaaaacct gataggtgag actacttcag tttattccag caagaaagat tgtgatgcaa 1820
 gatttctttc ttccctgagac aaaaaaaaaa aaaagaaaaa aaaatctttt caaaattttac 1880
 tttgtcaaat aaaaatttgt ttttcagaga tttaccaccc agttcatggt tagaaatatt 1940
 ttgtggcaat gaagaaaaca ctacggaaaa taaaaaataa gataaagcct t 1991

<210> 2

<211> 529

<212> PRT

<213> Homo sapiens

<400> 2

Met Ser Val Lys Trp Thr Ser Val Ile Leu Leu Ile Gln Leu Ser Phe
 1 5 10 15
 Cys Phe Ser Ser Gly Asn Cys Gly Lys Val Leu Val Trp Ala Ala Glu
 20 25 30
 Tyr Ser His Trp Met Asn Ile Lys Thr Ile Leu Asp Glu Leu Ile Gln
 35 40 45
 Arg Gly His Glu Val Thr Val Leu Ala Ser Ser Ala Ser Ile Leu Phe
 50 55 60
 Asp Pro Asn Asn Ser Ser Ala Leu Lys Ile Glu Ile Tyr Pro Thr Ser
 65 70 75 80
 Leu Thr Lys Thr Glu Leu Glu Asn Phe Ile Met Gln Gln Ile Lys Arg
 85 90 95
 Trp Ser Asp Leu Pro Lys Asp Thr Phe Trp Leu Tyr Phe Ser Gln Val
 100 105 110
 Gln Glu Ile Met Ser Ile Phe Gly Asp Ile Thr Arg Lys Phe Cys Lys
 115 120 125
 Asp Val Val Ser Asn Lys Lys Phe Met Lys Lys Val Gln Glu Ser Arg
 130 135 140
 Phe Asp Val Ile Phe Ala Asp Ala Ile Phe Pro Cys Ser Glu Leu Leu
 145 150 155 160
 Ala Glu Leu Phe Asn Ile Pro Phe Val Tyr Ser Leu Ser Phe Ser Pro
 165 170 175
 Gly Tyr Thr Phe Glu Lys His Ser Gly Gly Phe Ile Phe Pro Pro Ser
 180 185 190
 Tyr Val Pro Val Val Met Ser Glu Leu Thr Asp Gln Met Thr Phe Met
 195 200 205
 Glu Arg Val Lys Asn Met Ile Tyr Val Leu Tyr Phe Asp Phe Trp Phe
 210 215 220
 Glu Ile Phe Asp Met Lys Lys Trp Asp Gln Phe Tyr Ser Glu Val Leu
 225 230 235 240

10057834.0125002

Gly Arg Pro Thr Thr Leu Ser Glu Thr Met Gly Lys Ala Asp Val Trp
245 250 255
Leu Ile Arg Asn Ser Trp Asn Phe Gln Phe Pro His Pro Leu Leu Pro
260 265 270
Asn Val Asp Phe Val Gly Gly Leu His Cys Lys Pro Ala Lys Pro Leu
275 280 285
Pro Lys Glu Met Glu Asp Phe Val Gln Ser Ser Gly Glu Asn Gly Val
290 295 300
Val Val Phe Ser Leu Gly Ser Met Val Ser Asn Met Thr Glu Glu Arg
305 310 315 320
Ala Asn Val Ile Ala Ser Ala Leu Ala Gln Ile Pro Gln Lys Val Leu
325 330 335
Trp Arg Phe Asp Gly Asn Lys Pro Asp Thr Leu Gly Leu Asn Thr Arg
340 345 350
Leu Tyr Lys Trp Ile Pro Gln Asn Asp Leu Leu Gly His Pro Lys Thr
355 360 365
Arg Ala Phe Ile Thr His Gly Gly Ala Asn Gly Ile Tyr Glu Ala Ile
370 375 380
Tyr His Gly Ile Pro Met Val Gly Ile Pro Leu Phe Ala Asp Gln Pro
385 390 395 400
Asp Asn Ile Ala His Met Lys Ala Arg Gly Ala Ala Val Arg Val Asp
405 410 415
Phe Asn Thr Met Ser Ser Thr Asp Leu Leu Asn Ala Leu Lys Arg Val
420 425 430
Ile Asn Asp Pro Ser Tyr Lys Glu Asn Val Met Lys Leu Ser Arg Ile
435 440 445
Gln His Asp Gln Pro Val Lys Pro Leu Asp Arg Ala Val Phe Trp Ile
450 455 460
Glu Phe Val Met Arg His Lys Gly Ala Lys His Leu Arg Val Ala Ala
465 470 475 480
His Asp Leu Thr Trp Phe Gln Tyr His Ser Leu Asp Val Ile Gly Phe
485 490 495
Leu Leu Val Cys Val Ala Thr Val Ile Phe Ile Val Thr Lys Cys Cys
500 505 510
Leu Phe Cys Phe Trp Lys Phe Ala Arg Lys Ala Lys Lys Gly Lys Asn
515 520 525
Asp

<210> 3
<211> 20
<212> DNA
<213> Homo sapiens

<400> 3
gtgtcaatgg actgcagaac

20

<210> 4
<211> 20
<212> DNA
<213> Homo sapiens

<400> 4

cctttccaca attcccagag 20

<210> 5
<211> 20
<212> DNA
<213> Homo sapiens

<400> 5
cttggctaatt ttatctttgg 20

<210> 6
<211> 19
<212> DNA
<213> Homo sapiens

<400> 6
cccactaccc tgactttat 19

<210> 7
<211> 20
<212> DNA
<213> Homo sapiens

<400> 7
ggacataacc atgagaaatg 20

<210> 8
<211> 19
<212> DNA
<213> Homo sapiens

<400> 8
agctctgctt caaagacac 19

<210> 9
<211> 21
<212> DNA
<213> Homo sapiens

<400> 9
tgtccgtatg ctactattga a 21

<210> 10
<211> 21
<212> DNA
<213> Homo sapiens

<400> 10
tgtgctaatac cctttgtaaa t 21

0057834 042003

<210> 11
<211> 22
<212> DNA
<213> Homo sapiens

<400> 11
tttttttttc tattcctgtc ag 22

<210> 12
<211> 16
<212> DNA
<213> Homo sapiens

<400> 12
ctttacccca cccatt 16

<210> 13
<211> 20
<212> DNA
<213> Homo sapiens

<400> 13
cccttgatct cattcctact 20

<210> 14
<211> 24
<212> DNA
<213> Homo sapiens

<400> 14
aactggctat tcttttagatg tatg 24

<210> 15
<211> 25
<212> DNA
<213> Homo sapiens

<400> 15
cattcctact ctttatacag ttctc 25

<210> 16
<211> 17
<212> DNA
<213> Homo sapiens

<400> 16
cccccgattc agactat 17

```
<210> 17
<211> 20
<212> DNA
<213> Homo sapiens
```

```
<400> 17
cccttgatct cattcctact                20
```

```
<210> 18
<211> 24
<212> DNA
<213> Homo sapiens
```

```
<400> 18
aactggctat tcttttagatg tatg                24
```

```
<210> 19
<211> 18
<212> DNA
<213> Homo sapiens
```

<400> 19
tcctccgaag tctgaaac 18

```
<210> 20
<211> 24
<212> DNA
<213> Homo sapiens
```

<400> 20	
tataaaaaaag gatgaaactc acac	24

```
<210> 21
<211> 18
<212> DNA
<213> Homo sapiens
```

<400> 21	
caagccccca agttatgt	18

```
<210> 22
<211> 20
<212> DNA
<213> Homo sapiens
```

```
<400> 22
cagtaggatac cgcgatataa                20
```


<210> 23
 <211> 20
 <212> DNA
 <213> Homo sapiens

 <400> 23
 tctgaggggt tttgtctgta 20

 <210> 24
 <211> 20
 <212> DNA
 <213> Homo sapiens

 <400> 24
 ccgcgatata agttcaacaa 20

 <210> 25
 <211> 20
 <212> DNA
 <213> Homo sapiens

 <400> 25
 ggacataacc atgagaaatg 20

 <210> 26
 <211> 19
 <212> DNA
 <213> Homo sapiens

 <400> 26
 ttaagagcgg atgagttgt 19

 <210> 27
 <211> 20
 <212> DNA
 <213> Homo sapiens

 <400> 27
 tcatcatgca acagattaag 20

 <210> 28
 <211> 20
 <212> DNA
 <213> Homo sapiens

 <400> 28
 cactacaggg aaaaatagca 20

 <210> 29

<211> 20
<212> DNA
<213> Homo sapiens

<400> 29
accctttgtg tacagtctca 20

<210> 30
<211> 19
<212> DNA
<213> Homo sapiens

<400> 30
agctctgctt caaagacac 19

<210> 31
<211> 21
<212> DNA
<213> Homo sapiens

<400> 31
ttgcctacat tattctaacc c 21

<210> 32
<211> 17
<212> DNA
<213> Homo sapiens

<400> 32
ctttacccca cccattt 17

<210> 33
<211> 25
<212> DNA
<213> Homo sapiens

<400> 33
cattcctact ctttatacag ttctc 25

<210> 34
<211> 17
<212> DNA
<213> Homo sapiens

<400> 34
cccccgattc agactat 17

<210> 35
<211> 25

<212> DNA
 <213> Homo sapiens

 <400> 35
 cattcctact ctttatacag ttctc 25

 <210> 36
 <211> 17
 <212> DNA
 <213> Homo sapiens

 <400> 36
 cccccgattc agactat 17

 <210> 37
 <211> 18
 <212> DNA
 <213> Homo sapiens

 <400> 37
 tcctccgaag tctgaaac 18

 <210> 38
 <211> 23
 <212> DNA
 <213> Homo sapiens

 <400> 38
 tataaaaagg atgaaactca cac 23

 <210> 39
 <211> 20
 <212> DNA
 <213> Homo sapiens

 <400> 39
 tctgaggggt tttgtctgta 20

 <210> 40
 <211> 22
 <212> DNA
 <213> Homo sapiens

 <400> 40
 ttttttgtct caggaagaaa ga 22

 <210> 41
 <211> 24
 <212> DNA

<213> Homo sapiens

<400> 41

aaaaaaagaa aaaaaaatct tttc

24

<210> 42

<211> 20

<212> DNA

<213> Homo sapiens

<400> 42

ccgcgatata agttcaacaa

20

<210> 43

<211> 22

<212> DNA

<213> Homo sapiens

<400> 43

tgcattgcac caggatgtct gt

22

<210> 44

<211> 22

<212> DNA

<213> Homo sapiens

<400> 44

tgcattgcac caagatgtct gt

22

<210> 45

<211> 23

<212> DNA

<213> Homo sapiens

<400> 45

tcttggatga gcttattcag aga

23

<210> 46

<211> 23

<212> DNA

<213> Homo sapiens

<400> 46

tcttggatga gcctattcag aga

23

<210> 47

<211> 21

<212> DNA

<213> Homo sapiens

<400> 47
cattttgggtt atatttttca c 21

<210> 48
<211> 21
<212> DNA
<213> Homo sapiens

<400> 48
cattttgggtt ttatttttca c 21

<210> 49
<211> 21
<212> DNA
<213> Homo sapiens

<400> 49
cataactaga aagttctgta a 21

<210> 50
<211> 21
<212> DNA
<213> Homo sapiens

<400> 50
cataactagg aagttctgta a 21

<210> 51
<211> 20
<212> DNA
<213> Homo sapiens

<400> 51
cctggctaca cttttgaaaa 20

<210> 52
<211> 20
<212> DNA
<213> Homo sapiens

<400> 52
cctggctaca tttttgaaaa 20

<210> 53
<211> 21
<212> DNA
<213> Homo sapiens

<400> 53
gaagacccac tacattatct g 21

<210> 54
<211> 21
<212> DNA
<213> Homo sapiens

<400> 54
gaagacccac tacggtatct g 21

<210> 55
<211> 26
<212> DNA
<213> Homo sapiens

<400> 55
aattttcagt ttccatatcc actctt 26

<210> 56
<211> 26
<212> DNA
<213> Homo sapiens

<400> 56
aattttcagt ttccatcatcc actctt 26

<210> 57
<211> 22
<212> DNA
<213> Homo sapiens

<400> 57
taggtctcaa tactcggctc ta 22

<210> 58
<211> 22
<212> DNA
<213> Homo sapiens

<400> 58
taggtctcaa tactcggctg ta 22

<210> 59
<211> 19
<212> DNA
<213> Homo sapiens

<400> 59

10057534 042007

tacaagtgga taccccaga 19

<210> 60
<211> 19
<212> DNA
<213> Homo sapiens

<400> 60
tataagtgga taccccaga 19

<210> 61
<211> 26
<212> DNA
<213> Homo sapiens

<400> 61
gggagaaaga atacattata attttt 26

<210> 62
<211> 25
<212> DNA
<213> Homo sapiens

<400> 62
gggagaaaga atacttataa ttttt 25

<210> 63
<211> 21
<212> DNA
<213> Homo sapiens

<400> 63
ttccattggt tgccgatcaa c 21

<210> 64
<211> 21
<212> DNA
<213> Homo sapiens

<400> 64
ttccattggt tgctgatcaa c 21

<210> 65
<211> 21
<212> DNA
<213> Homo sapiens

<400> 65
gaatgcattg aagagagtaa t 21

400 21 22 19 19 20

<210> 66
<211> 21
<212> DNA
<213> Homo sapiens

<400> 66
gaatgcattg cagagagtaa t 21

<210> 67
<211> 22
<212> DNA
<213> Homo sapiens

<400> 67
ctggtctgtg tggcaactgt ga 22

<210> 68
<211> 22
<212> DNA
<213> Homo sapiens

<400> 68
ctggtctgtg tggcgactgt ga 22

<210> 69
<211> 19
<212> DNA
<213> Homo sapiens

<400> 69
taagataaag ccttatgag 19

<210> 70
<211> 19
<212> DNA
<213> Homo sapiens

<400> 70
taagataaag acttatgag 19

<210> 71
<211> 20
<212> DNA
<213> Artificial Sequence

<400> 71
tctgagcatg tggatggcaa 20


```
<210> 72
<211> 20
<212> DNA
<213> Artificial Sequence
```

```
<220>
<223> Description of Artificial Sequence:  Synthetic
      Primer
```

```
<210> 73
<211> 22
<212> DNA
<213> Artificial Sequence
```

```
<400> 73
gaagcaaatt ctttcttcac ag                22
```

```
<210> 74
<211> 21
<212> DNA
<213> Artificial Sequence
```

```
<400> 74
accagtaagg cacttcatct t                                     21
```

```
<210> 75
<211> 22
<212> DNA
<213> Artificial Sequence
```

```
<400> 75
cgatttcagac tataaaagaat gt                22
```

```
<210> 76
<211> 17
```

4007462906

<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
Primer

<400> 76
tcctccgaag tctgaac

17

<210> 77
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
Primer

<400> 77
ccacctagtg aaaaatattg ttc

23

<210> 78
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
Primer

<400> 78
atcacaatct ttcttgctgg a

21